MEDICINES FOR THE PEOPLE

2020
ANNUAL
REPORT

DNDi
Drugs for Neglected Diseases *initiative*

FOREWORD

From the Chair of the Board and the Executive Director

Dr Marie-Paule Kieny
Chair of the Board of Directors

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Executive Director

2020 will be forever remembered for the tragic loss and devastating disruption the COVID-19 pandemic brought to bear on families and communities around the world. While the scientific response to COVID-19 is enabling major advances and the development of new health technologies at unprecedented speed, millions of people remain without access to the vaccines, diagnostics, and treatments needed to save lives and guard against new waves of infection.

From the start of the pandemic, DND*i* teams have been mobilizing our networks and leveraging our experience in needs-driven, non-profit research and development (R&D) to accelerate research and equitable access to health tools in low-resource settings.

In April 2020, we co-founded the **COVID-19 Clinical Research Coalition**, which has brought together more than 800 researchers, physicians, funders, and policymakers from 88 countries to advance research that answers to the specific needs of people and health systems in low- and middle-income countries (LMICs). And in November, we launched **ANTICOV**, an adaptive platform trial in 13 African countries testing multiple early treatment options for mild-to-moderate COVID-19. Conducted with a consortium of 25 organizations from Africa and around the world, we aim to identify one or two safe, effective, and affordable treatments that can limit progression to severe disease and prevent fragile health systems from being overwhelmed by surges in hospitalization.

Our **drug discovery** teams are also contributing to the response, working with partners to identify potential treatment candidates from existing antivirals while also initiating longer-term efforts to discover all-new antiviral drug candidates for the treatment of SARS-CoV-2, future generations of coronavirus, and potentially other pandemic-prone viruses. And from the earliest days of the pandemic, we have spoken out – advocating for R&D to be driven by the public interest and for COVID-19 health tools to be developed and delivered as public goods, with equitable access for all.

2020 is also a year that we will look back on with pride for the tremendous momentum our teams and partners maintained across more than 40 R&D projects, standing firm in our commitment to neglected patients against unforeseen challenges and difficult odds.

In late 2020, our industrial partner Pharmaniaga submitted ravidasvir for the treatment of hepatitis C for regulatory approval in Malaysia, where we have worked with partners since 2016 to conduct clinical trials and pilot 'test-and-treat' strategies that have connected thousands of people to life-saving treatment. Granted conditional approval in June 2021, the all-new chemical entity will now be part of an affordable, safe, and highly effective all-oral cure for hepatitis C. **Ravidasvir is the ninth treatment delivered by DND*i*** since our founding and stands out as the first drug for hepatitis C to be developed through South-South collaboration.

Our teams and partners in the Democratic Republic of Congo (DRC) and Guinea brought us one step closer to reaching our long-term objective for people affected by sleeping sickness, completing post-treatment follow-up for all participants in our pivotal Phase II/III clinical trial of acoziborole. The single-dose oral drug for both stages of the disease holds tremendous promise as a tool to enable the **sustainable elimination of sleeping sickness** and reach patients in even the most remote communities.

As we pushed forward on our R&D and access agenda and lent our capacities in the response to COVID-19, so too did we cement our commitments to driving medical innovation and access for neglected patients in the years to come, launching our **new Strategic Plan**. It charts our course to 2028, by which time we aim to deliver an additional 15 to 18 new treatments, for a total of 25 treatments in our first 25 years. In delivering on our mission, we will double down on neglect with a proactive agenda for maternal and child health, gender-responsive R&D, and climate-sensitive and pandemic-prone diseases, while leveraging new technologies to accelerate R&D and access.

Please join us as we continue to use the **power of our partnerships** to deliver medicines for life-threatening diseases that disproportionately impact poor and marginalized people, strengthen innovation ecosystems that put people's needs first, and speak out for the policies and political will needed to leave no one behind.

We invite you to learn more about our ambitions and vision for the road ahead – and we thank the many friends, partners, and supporters who have propelled our progress so far.

2020 in numbers

Research and development (R&D) portfolio

40+
projects in our R&D portfolio

20+
new chemical entities in DNDi's drug development pipeline

92,360
chemical compounds screened for new drug potential

Maximizing the partnership model

4.6:1
ratio of partners vs DNDi FTEs*

14:1
ratio of partner vs DNDi FTEs* in Africa

Clinical trials

22
clinical trials in 8 disease areas at 83 sites in 28 countries

3,140
patients enrolled in active DNDi clinical studies

49%
of patients enrolled are children

Contributions and expenditure

EUR 56 MILLION
in multi-year funds secured

EUR 5 MILLION
in-kind contributions and collaborative funding from partners

89%
of expenditure on social mission to maximize impact for neglected patients

Sharing knowledge

46
peer-reviewed scientific publications on DNDi's research

98%
published in open-access journals

50%
had a female lead or co-lead author

74%
had at least one author from a partner institution in an endemic country

Fostering sustainable solutions

1,275
people trained to support clinical research in Africa, Asia, and Latin America

66%
of all R&D partner FTEs* are in Africa

* Staff in full-time equivalents

DND*i* ACHIEVEMENTS SINCE 2003

TREATMENTS DELIVERED

9 field-adapted and affordable treatments* for 6 deadly diseases, including ASAQ for malaria (with over 500 million treatments distributed since 2007), fexinidazole, the first all-oral treatment for sleeping sickness and DND*i*'s first new chemical entity, and ravidasvir, the first drug for hepatitis C to be developed through South-South collaboration.

R&D PIPELINE REPLENISHED

20+ new chemical entities in DND*i*'s portfolio.

4 million+ compounds screened.

Mature portfolio with 13 projects in Phase III or under regulatory review.

POLICIES INFLUENCED

DND*i*'s model, experience, and lessons learned documented and disseminated to influence multiple policy processes – from WHO, G7/G20, and the United Nations to national and regional policy forums and funders – particularly around core principles and practices that enable needs-driven R&D and equitable access, such as open and transparent sharing of research knowledge, data and R&D costs, and pro-access management of intellectual property and licensing.

CLINICAL TRIALS CONDUCTED

An average of 20 active clinical studies from Phase I to Phase IV ongoing – located mostly in LMICs – with more than 2,500+ patients enrolled at any given time.

GLOBAL PARTNERSHIPS FORGED

200+ partner institutions in 40+ countries have joined DND*i* to deliver the best science for the most neglected.

RESEARCH NETWORKS ESTABLISHED

4 clinical research networks created for target diseases in Africa and Latin America, bringing together 500+ researchers across institutions in dozens of LMICs to support and strengthen R&D capacity, promote scientific exchange, and facilitate access to new treatments.

COVID-19 Clinical Research Coalition with 800+ members working to fast-track research for tools adapted to the needs of patients and health systems in resource-limited settings.

DIVERSE GLOBAL TEAM MOBILIZED

A diverse global team of 250+ staff driving research, partnerships, and advocacy across 9 organizational hubs in Cape Town, Geneva, Kinshasa, Kuala Lumpur, Nairobi, New Delhi, New York, Rio de Janeiro, and Tokyo.

NEW ORGANIZATION TO FIGHT DRUG-RESISTANT INFECTIONS CREATED

DND*i* joined forces with the World Health Organization (WHO) in 2016 to create the Global Antibiotic R&D Partnership (GARDP), now an independent organization developing new treatments for drug-resistant infections that pose the greatest threat to health. Both organizations continue to share R&D expertise and capacity, as well as a common approach on global health policy for promoting and contributing to public health needs-driven R&D and access.

* As of July 2021

THE ROAD AHEAD: OUR NEW STRATEGIC PLAN

25 treatments in 25 years

DND*i* was created in response to the frustration of clinicians and the desperation of patients faced with medicines that were ineffective, unsafe, unavailable, unaffordable, or that had never been developed at all.

Nearly two decades later, DND*i* has grown into a network of more than 200 partner institutions that spans the globe, united in our pursuit of science driven by collaboration, not competition, and by patients' needs, not profits. Together, we have delivered nine field-adapted and affordable treatments for six deadly diseases, saving millions of lives.

In 2020, dozens of partners and donors who have propelled our work since 2003 joined us to take stock of our progress and accompany our teams in plotting an ambitious course of action for neglected patients for the years ahead.

Our new 2021-2028 Strategic Plan charts an eight-year journey to deliver 15 to 18 new treatments, for a total of 25 new treatments in our first 25 years.

Our work will contribute directly to achieving the Sustainable Development Goals, including Universal Health Coverage; multi-sector 'One Health' approaches for disease control and elimination; and WHO strategies, including the 2030 Roadmap for Neglected Tropical Diseases (NTDs). A key measure of our shared progress in meeting these ambitions will be the extent to which health systems provide healthcare for all, including women, children, the poor, people with neglected or stigmatizing diseases, and those at the margins of society.

Please join us.

FIND OUT MORE

COMMITMENTS: 2021–2028

DRIVE IMPACT ACROSS THE 3 PILLARS OF OUR MISSION

- INNOVATE TO SAVE LIVES
- FOSTER INCLUSIVE & SUSTAINABLE SOLUTIONS
- ADVOCATE FOR CHANGE

FOCUS ON 5 CROSS-CUTTING STRATEGIC IMPERATIVES

1. Deliver new treatments and expand access for neglected patients by addressing R&D gaps for NTDs and viral diseases, including pandemic-prone and climate-sensitive diseases
2. Join with public health leaders and R&D actors in LMICs to advance sustainable innovation ecosystems that address neglected patients' needs
3. Contribute to building a proactive agenda for maternal and child health and gender-responsive R&D
4. Champion open science and transparency
5. Leverage new technologies to accelerate R&D and access

DELIVER 15–18 ADDITIONAL TREATMENTS

10-12 new treatments from current mature portfolio (2021-2024)
5-7 new treatments from earlier-stage new chemical entities and portfolio expansion (2025-2028)

FROM BENCH TO BEDSIDE

DND*i* research & development portfolio

Acting as a 'conductor of a virtual orchestra', we collaborate with research partners around the world at all stages of the R&D process. Our R&D portfolio includes 48 projects and more than 20 new chemical entities for 8 disease areas (as of December 2020).

FIND OUT MORE

	DISCOVERY			TRANSLATION			DEVELOPMENT		IMPLEMENTATION
	Screen	Hit-to-lead	Lead optimization	Pre-clinical	Phase I	Phase IIa/Proof-of-concept	Phase IIb/III	Registration	Treatment access
Sleeping sickness			SCYX-13330682 SCYX-1608210 ⊕				Acoziborole ⊕ Fexinidazole for *T.b. rhodesiense* ⊕		**Fexinidazole** for *T.b. gambiense** ⊕ **Nifurtimox-eflornithine combination therapy** (NECT)*
Leishmaniasis	Screening	Leishmaniasis Hit-to-lead NTD Drug Discovery Booster Hit-to-lead	S07 series ⊕ CF series ⊕	DNDI-6174 ⊕	DNDI-6148 ⊕ DNDI-0690 ⊕ GSK899 / DDD853651 ⊕ Novartis LXE408 ⊕ CpG-D35 for CL ⊕ GSK245 / DDD1305143 ⊕		New CL combination New treatments for PKDL Miltefosine + paromomycin combination (Africa)	New VL treatments (Latin America) New treatments for HIV/VL	**SSG&PM** (East Africa)* **New VL treatments** (South Asia)*
Chagas disease	Screening	Chagas disease Hit-to-lead NTD Drug Discovery Booster Hit-to-lead	Oxaborole profiling ⊕ UW series ⊕ Daiichi Sankyo series ⊕	Biomarkers		Fexinidazole ⊕	New benznidazole regimens ⊕		**Benznidazole** paediatric dosage forms*
Filaria: River blindness				CC6166 ⊕	Oxfendazole ⊕	Emodepside ⊕ TylAMac (ABBV-4083) ⊕			
Mycetoma							Fosravuconazole ⊕		
HIV					5 FC (cryptococcal meningitis)			4-in-1 (ABC/3TC/LPV/r)	**Super-booster therapy** for children with HIV/TB* 2-in-1 LPV/r pellets and ABC/3TC or AZT/3TC
Hepatitis C							Ravidasvir + sofosbuvir ⊕	Ravidasvir ⊕	
COVID-19		Hit-to-lead broad-spectrum antivirals		Pre-clinical support			ANTICOV		
Malaria**									**Fixed-dose combination ASMQ*** **Fixed-dose combination ASAQ***

⊕ *New chemical entity;* **Treatments delivered by DNDi;* ***Implementation transferred to the Medicines for Malaria Venture in 2015.*

SLEEPING SICKNESS

Delivering breakthrough treatments and expediting access to eliminate the disease – for good

Sleeping sickness – or human African trypanosomiasis (HAT) – is a parasitic disease spread by the bite of the tsetse fly. Over time, it causes severe neuropsychiatric symptoms and is almost always fatal if left untreated. Until 2008, the only treatment available for advanced sleeping sickness was melarsoprol, an arsenic derivative so toxic it killed 1 in 20 patients.

FIND OUT MORE

SLEEPING SICKNESS statistics

8.5 MILLION
people live in areas of moderate to very high risk

90 %
reduction in reported cases from 2009 to 2019

62 %
of reported cases in 2019 were in the DRC

The push for progress

We have been focused on developing better treatments for sleeping sickness since our founding in 2003. By 2009, working closely with partners, we finalized the development of nifurtimox and eflornithine (NECT), a simpler, safer treatment for the second stage of the most common form of the disease. In 2018, DND*i* and our partners delivered fexinidazole, a paradigm-changing simple oral treatment for both stages of the disease that can be taken at home. And we have helped build the HAT Platform, a network of 120 experts from over 20 research institutions in affected countries, closely linked with policymakers, working to increase diagnosis, care, treatment, and research so that new treatments can be rapidly and effectively evaluated, registered, and rolled out.

Our goal is now to complete development of and then ensure access to acoziborole, a single-dose oral treatment that holds tremendous promise for efforts to sustainably eliminate the disease. We will also continue work to scale up access to fexinidazole while studying its use for *T.b. rhodesiense* sleeping sickness, a less common but more acute form of the disease.

Fexinidazole

The first deliveries of fexinidazole for use outside of clinical trials began in the DRC in January 2020. DND*i* teams continued to support the roll-out of the new all-oral treatment through access and pharmacovigilance activities in Angola, Central African Republic, the DRC, Guinea, and South Sudan. Our Phase II/III study of fexinidazole for treatment of *T.b. rhodesiense* sleeping sickness continued in Malawi, while the start of recruitment in Uganda was delayed to 2021 due to the COVID-19 pandemic.

Acoziborole

In August 2020, post-treatment follow-up was completed for all 208 patients recruited in the DRC and Guinea for DND*i*'s pivotal Phase II/III clinical trial, which evaluated the safety and efficacy of acoziborole as a potential treatment for both Stage 1 and Stage 2 *T.b. gambiense* sleeping sickness. A final study report will be prepared in 2021. Additional non-clinical studies to meet European Medicines Agency and US Food and Drug Administration requirements were also carried out.

“ My son’s health had worsened over a period of six months: he was sleepy all the time, had high fevers, and lacked appetite – and he became increasingly nervous and progressively weaker. ”

Guy Bongongo’s father describes his 12-year-old son’s experience with sleeping sickness before being treated with fexinidazole after it first became available for use in the DRC in early 2020. Guy was treated at Mushie General Hospital in Mai-Ndombe Province. Everything went very well for the young boy, who is now completely cured.

LEISHMANIASIS

Delivering safer, simpler treatments to save lives and reduce social stigma

Caused by parasites transmitted by the bite of a sandfly, leishmaniasis has strong links to poverty, taking its heaviest toll on people affected by malnutrition, poor housing, and displacement. Visceral leishmaniasis (VL) – also known as kala-azar – causes fever, weight loss, spleen and liver enlargement, and, if not treated, death. Cutaneous leishmaniasis (CL) leaves life-long scars, mostly on the face, causing social stigma, particularly for women and children. Current treatments differ from region to region, but all either require hospital stays or complex infusions, or consist of drugs with serious side effects.

FIND OUT MORE: VISCERAL LEISHMANIASIS | CUTANEOUS LEISHMANIASIS

> **“ Two of my children were healed with the current kala-azar treatment, but the injections are very painful. My only wish would be for the current injections-based treatment to be swapped with tablets. ”**

Mary is a mother and farmer from West Pokot, Kenya. Learn more about her family's experience with kala-azar.

MARY'S STORY

LEISHMANIASIS statistics

600 MILLION
people at risk of VL across the globe

2,000X
risk of developing active VL for people living with HIV

600,000-1 MILLION
new cases of CL each year

The push for progress

With our partners, DND*i* has developed improved VL treatments that are now part of national treatment guidelines in East Africa as well as South Asia, where elimination efforts have contributed to a sharp decline in cases. Additionally, we have replenished the R&D pipeline with an unprecedented portfolio of all-new potential drugs. The Leishmaniasis East Africa Platform, founded by DND*i* in 2003, has helped drive progress against the disease in Ethiopia, Kenya, Uganda, and Sudan. Our collaborations have also identified several promising compounds for CL that are now in different stages of development. In 2014, we established redeLEISH, a network of CL experts working across 90 institutions in 20 countries to share know-how and to design and conduct vital clinical research.

Our goal is now to deliver new, short-course oral treatments for both forms of leishmaniasis, including combinations of new chemical entities, that are safe and easier to manage at the primary healthcare level, with the goal of bringing prompt diagnosis and treatment closer to patients.

Momentum toward all-new, all-oral treatments

In addition to our near-term goals for delivering improved, short-course treatments for leishmaniasis with existing drugs, our partnerships are making strides toward realizing our ultimate objective of delivering two or three safe, effective, and affordable all-oral drug regimens that can be easily deployed at the primary healthcare level. This continued progress is thanks to a strong consortium of R&D partners including the University of Dundee, Novartis, GSK, Anacor/Pfizer, Takeda Pharmaceutical Company Limited, Eisai, and TB Alliance – and thanks to financial support from the Global Health Innovative Technology Fund, Wellcome, the European and Developing Countries Clinical Trials Partnership (EDCTP), and others.

In 2020, our teams and partners continued to advance an unprecedented portfolio of all-new chemical entities for leishmaniasis, which includes seven drug candidates from six distinct classes, each with a novel mechanism of action, as well as others in earlier stages of development. Phase I studies in healthy volunteers were initiated or continued for DNDI-0690, DNDI-6148, GSK899/DDD853651, and GSK245/DDD1305143 – as well as LXE408, a first-in-class compound that we are developing jointly with Novartis following a collaboration agreement reached in early 2020. Pre-clinical studies of the novel 'immunomodulator' CpG-D35 for CL were completed in late 2020, with studies in healthy volunteers planned to start in 2021. Preparations to initiate pre-clinical activities in partnership with Eisai continued for DNDI-6174.

Better VL treatments in East Africa

Safer, simpler alternatives to the current standard treatment used for VL in East Africa are urgently needed – particularly for children, who represent up to 70% of the population at risk in the region. While a significant improvement over previous options, the current treatment requires two painful daily injections, as well as hospitalization for the entirety of the 17-day treatment period.

Following positive outcomes from earlier studies in South Asia using the combination of oral miltefosine and paromomycin (MF+PM), DND*i* together with partners in the AfriKADIA consortium launched a Phase III trial in 2018 to study two MF+PM regimens against the current standard treatment. Study enrolment was completed in May 2020, with 439 participants enrolled across seven study sites in Ethiopia, Kenya, Sudan, and Uganda – more than 70% of whom were children. Study results are expected in late 2021, following the completion of monitoring visits and data analysis.

LEISHMANIASIS

HIV/VL co-infection: Building evidence for better treatment recommendations

People living with HIV have a 2,000 times greater risk of developing active VL. HIV affects VL by altering its severity, worsening treatment outcomes and relapse rates, and increasing the risk of death. Co-infection remains prevalent in several parts of the world, notably in North-West Ethiopia, where 20 to 40% of VL cases occur in people living with HIV.

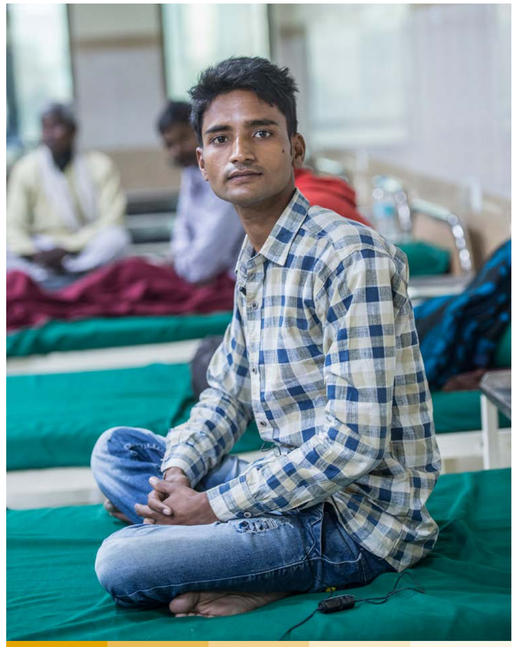
In 2011, in an effort to improve treatment options, Médecins Sans Frontières (MSF) began administering a new combination regimen – liposomal amphotericin B with the oral drug miltefosine – under compassionate use to co-infected patients in Abdurafi Health Centre in North-West Ethiopia. Following promising results, DND*i* and partners conducted a Phase III study to compare the combination regimen to treatment with liposomal amphotericin B alone (the current recommended treatment). Results from patients treated at two clinics in Ethiopia demonstrated high efficacy, with a cure rate of 67% for the 28-day course. The cure rate rose to 88% when patients who were not cured after 28 days received a second round of treatment to clear the parasite, with the total treatment lasting 58 days.

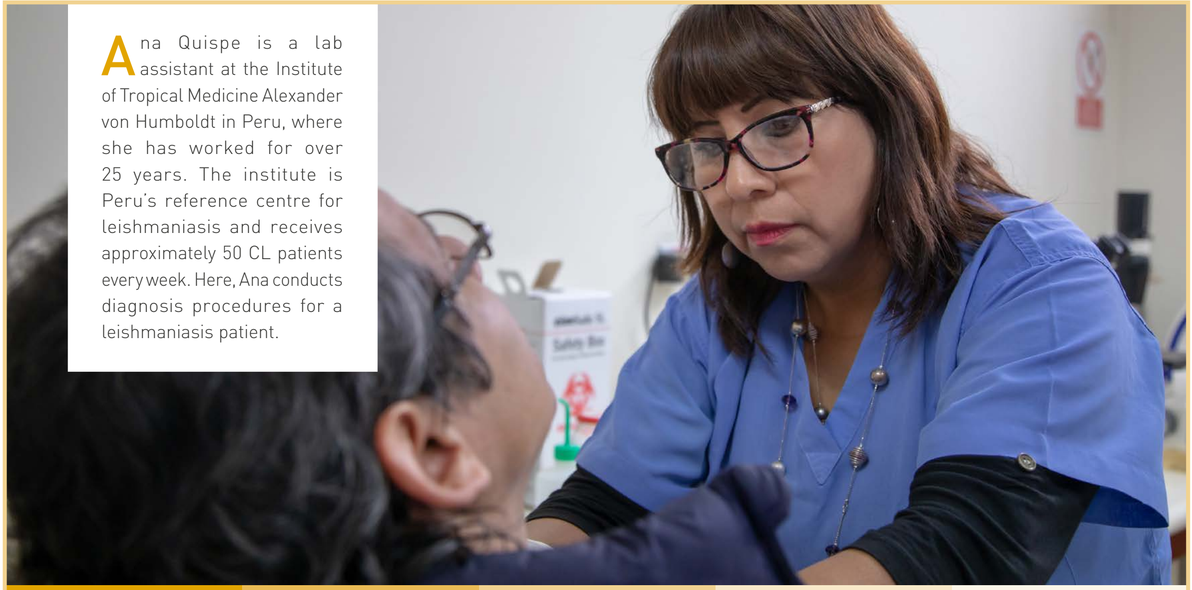
In 2020, the WHO Guideline Development Group began evaluating HIV/VL co-infection treatment recommendations for South Asia and East Africa; updated recommendations are expected in 2021.

Post-kala-azar dermal leishmaniasis: The disease that strikes back

Post-kala-azar dermal leishmaniasis (PKDL) – a complication of VL that appears as a rash or skin condition months or years after successful VL treatment – is not deadly but can be highly stigmatizing.

Our Phase II study in Sudan testing both liposomal amphotericin B in combination with miltefosine, and paromomycin in combination with miltefosine, completed enrolment of 110 participants in May 2020. Patient follow-up will continue through the first half of 2021; results are expected by the end of 2021. Patient follow-up for our Phase II study in India to assess the safety and efficacy of liposomal amphotericin B monotherapy and a combination of liposomal amphotericin B and miltefosine continued through 2020. Results are expected in 2021, after completion of a 24-month follow-up period.





Ana Quispe is a lab assistant at the Institute of Tropical Medicine Alexander von Humboldt in Peru, where she has worked for over 25 years. The institute is Peru's reference centre for leishmaniasis and receives approximately 50 CL patients every week. Here, Ana conducts diagnosis procedures for a leishmaniasis patient.

CUTANEOUS LEISHMANIASIS

Shorter, safer, more effective treatment to replace toxic antimonials

Current treatments for CL are costly, and often require weeks of painful injections of toxic drugs called antimonials. Despite their severe side effects, these drugs have been used to treat the disease for nearly 70 years.

Using a combination of existing therapeutic approaches that excludes antimonials may improve outcomes for patients and reduce both side effects and treatment duration. DND*i*'s Phase II study completed in 2019 showed that a combination of thermotherapy (applying heat to a patient's lesion) with a shorter course of oral miltefosine is significantly better than thermotherapy alone for the treatment of uncomplicated CL in the Americas.

In 2020, DND*i* continued preparations for a Phase III study of the combination taking place in Bolivia, Brazil, Panama, and Peru together with DND*i*'s Brazilian research partner, the Oswaldo Cruz Foundation (Fiocruz), and with financial support from Brazil's Ministry of Health and National Council for Scientific and Technological Development (CNPq). The first participants were enrolled in the study in early 2021, and results are expected in early 2023.

Stimulating the immune system's response to fight infection

Leishmania parasites are able to persist in human cells by evading or exploiting immune mechanisms. Together with partners GeneDesign, an Ajinomoto company, and with financial support from Japan's Global Health Innovative Technology Fund, our teams are developing CpG-D35 as a therapeutic 'booster' to promote the immune system's response to the parasitic infection that causes CL and improve the efficacy of existing drugs.

Pre-clinical toxicology studies were completed in late 2020 and demonstrated the suitability of CpG-D35 to progress to first-in-human clinical trials. Clinical and pharmaceutical development will continue in 2021 with the initiation of a single ascending dose study in healthy volunteers.

CHAGAS DISEASE

Searching for shorter, safer, more effective treatments for a silent killer

Spread mainly by the bite of the 'kissing bug', Chagas disease is the biggest parasitic killer in the Americas. Although the disease can go unnoticed for years, it eventually causes irreversible damage to the heart and other vital organs in many affected patients. An estimated 70 million people are at risk and over 6 million live with Chagas worldwide, but by some estimates, only 1% of those infected have access to diagnosis and treatment. While effective, current treatments for the disease were discovered over 50 years ago, last at least eight weeks, and sometimes have serious side effects.

FIND OUT MORE

> "If treatment were shorter, more people would be willing to get it."

Magalí Arcazar lives in Tiquipaya, Cochabamba, Bolivia. She was diagnosed with Chagas when she went to donate blood. She finished the full course of treatment even though she experienced an allergic reaction due to sun exposure.

CHAGAS DISEASE statistics

>6 MILLION
people living with Chagas

21 COUNTRIES
The disease is endemic in 21 countries in Latin America

33% OF PEOPLE
infected suffer cardiac damage

The push for progress

Together with our partners, DND*i* delivered the first formulation of the drug benznidazole for infants and children in 2011, and later piloted a simplified model of care for people with Chagas, promoting test-and-treat approaches in Colombia that are now being replicated elsewhere in Latin America. In 2009, we established the Chagas Clinical Research Platform, a network of over 450 members in 25 countries working to conduct clinical trials and advocate for access to diagnosis and treatment for people most at risk.

Our goal is now to improve current treatments in the near-term by developing a safer, shorter treatment using benznidazole. We also aim to limit mother-to-child transmission and reach people living with Chagas disease with wider roll-out of 'test-and-treat' strategies. Longer term, our objective is to identify entirely new drug candidates and to initiate the clinical development of at least two compounds, with the aim of launching at least one Phase III trial resulting from this earlier-stage research by 2028.

Cutting treatment time by 75%

Our teams and partners began work in 2016 to identify shorter Chagas treatment regimens that are at least as effective as today's standard eight-week treatment with benznidazole, but with fewer side effects. Making treatment easier for patients to complete could remove a major barrier to treatment scale-up and bring new hope for people with Chagas disease.

Results from our Phase II BENDITA study (Benznidazole New Doses Improved Treatment and Associations), published *in The Lancet Infectious Diseases* in 2021, indicate comparable efficacy and improved safety of shorter regimens of benznidazole. A two-week course of treatment was particularly promising compared to the standard eight-week treatment, showing 79% efficacy at 12 months of follow-up, with no patients discontinuing treatment due to side effects.

Following these positive results, in collaboration with partners Mundo Sano Foundation and ELEA, our teams are now preparing to initiate a Phase III study in Argentina in 2021 to compare the efficacy and safety of the two-week treatment of benznidazole to the standard eight-week treatment.

DND*i* teams are also now collaborating on a wider regional initiative to interrupt mother-to-child transmission of Chagas disease – led by Fiocruz with financial support from Unitaid. The initiative will include a Phase III study of the shorter benznidazole regimen in Colombia, Bolivia, and Brazil.

Breaking down barriers to diagnosis and treatment

Through the Chagas Access Project, launched in 2015, DND*i* teams have been working with the Ministry of Health and Social Protection and the National Institute of Health in Colombia – and, later, with partners in Brazil, Guatemala, and Mexico – to implement customized solutions to help overcome barriers to diagnosis and treatment of Chagas disease.

In 2020, we implemented '4D' pilot projects to scale up diagnosis and treatment in two new municipalities in Boyacá state, Colombia, supported the creation of two new centres for diagnosis and treatment, and continued efforts to build awareness of the importance of early diagnosis in all pilot project communities. Together with FIND, we also supported Colombia's National Health Institute to validate simple rapid diagnostic tests for Chagas disease.

The Chagas Access Project expanded to Guatemala in 2020, where we are now working to boost diagnosis and treatment in Jutiapa department – including by supplying diagnostic kits and other essential equipment for a diagnostics validation study being conducted by the National Reference Laboratory of Guatemala.

FILARIA: RIVER BLINDNESS

Developing a rapid cure for millions at risk

Onchocerciasis – or river blindness – is a filarial disease caused by a parasitic worm transmitted by the bite of blackflies. While not life-threatening, it can result in long-term suffering and chronic illness, including visual impairment and blindness. Current prevention efforts are based on mass administration of the drug ivermectin, which, while highly effective in reducing transmission of the disease, must be administered every year for 10 years or more because it only kills juvenile worms and not the adults. It also cannot be used in people infected with another worm, African eye worm, because of the risk of potentially fatal side effects.

FIND OUT MORE

“ I depend totally on my family to feed and dress me. My wife doesn’t have a job. After I lost my sight, we couldn’t send any of our children to school. ”

Akoyo Osumaka was a fisherman before he fell ill with river blindness and lost his sight completely. Here, Akoyo is guided by his son, Aito, as they walk in the village of Babagulu, DRC. Aito had to quit his job in order to care for his father.

RIVER BLINDNESS statistics

ABOUT 205 MILLION
people at risk

21 MILLION
people infected with river blindness

>1 MILLION
people with vision loss

The push for progress

New tools that permanently sterilize or kill the adult worms that cause river blindness are needed to break the cycle of transmission and support elimination of the disease. We have built a portfolio of four R&D projects for river blindness and are advancing the development of new drug candidates together with our partners. DND*i* has also joined forces with the Helminth Elimination Platform (HELP), a consortium of research institutes, universities, NGOs, and pharmaceutical companies committed to developing new treatments for infections caused by parasitic worms.

Our goal is now to identify one or a combination of new drug candidates, complete Phase II trials, and to launch a Phase III confirmatory trial that we hope will result soon after in a new treatment option for onchocerciasis. Our research efforts will also support the development of diagnostic tools for river blindness, which are urgently needed.

Advancing four new drug candidates for river blindness

In 2020, DND*i* laid the groundwork for two Phase II trials to study the safety and efficacy of two potentially macrofilaricidal drugs: emodepside (under development with Bayer AG and partners) and TylAMac (under development with AbbVie and partners). DND*i* teams completed renovation of three clinical trial sites in preparation for the studies: one in Hohoe, Ghana (for the emodepside study) and two in the DRC (for the TylAMac study), one in Kimpese, Kwilu province and one in Masi-Manimba, Bas-Congo province.

Following Phase I trials of the drug candidate oxfendazole conducted by the Oxfendazole Development Group under the auspices of the US National Institute of Allergy and Infectious Diseases, the HELP consortium is now preparing to conduct a bioavailability Phase I trial in Tanzania to evaluate the safety, tolerability, and pharmacokinetics of a solid, field-adapted tablet developed by DND*i*. Preparatory work toward pre-clinical development of CC6166 – another potentially macrofilaricidal compound – also began in 2020.

From sleeping sickness to river blindness

Sustainable solutions for research in resource-limited settings

The Masi-Manimba referral hospital in the DRC has long been a principal clinical research site for DND*i* sleeping sickness research. The same site is now hosting our Phase II trial of TylAMac for river blindness, a disease that is also prevalent in the area. To leverage hospital staff’s many years of experience conducting clinical research, DND*i* teams worked to upgrade the facility in 2020 – constructing a new building and renovating existing ones – and trained staff to run trials for river blindness. The newly renovated site was inaugurated early 2021 and enrolled the first participants in the new study in May.

MYCETOMA

Conducting the world's first clinical trial

One of the world's most neglected diseases, mycetoma is a devastating, slow-growing infection most likely transmitted by a thorn prick. Occurring across the so-called 'mycetoma belt', which stretches from Central and South America to the Sahel, the Middle East, and South Asia, the fungal version of mycetoma leads to horrible deformities and disability. Currently, people living with mycetoma are confronted with ineffective, toxic, and overpriced drugs. For many, the only option is amputation.

FIND OUT MORE

El Safi is a singer, musician, and a father of six from Western Sudan and a patient at the Mycetoma Research Centre (MRC) in Khartoum. His long-standing foot mycetoma went untreated for a long period of time, and he had no choice but to undergo a below-knee amputation. He gradually recovered, and the MRC supported him to be fitted with a limb prosthesis and provided the equipment he needed to establish a small workshop in order to build a new life.

Despite the challenges he faces, El Safi regularly visits the MRC, playing and singing for the patients to improve their morale and encouraging them to continue their treatment to avoid his sad outcome.

MYCETOMA statistics

ONLY **35%**
cure rate for fungal mycetoma with current treatments

Unknown global burden

Occurs most often in the so-called **'mycetoma belt'** between latitudes 15° S and 30° N

The push for progress

DND*i* is running the world's first and only randomized comparative clinical trial for mycetoma, working with our partners on a safe, effective, and affordable treatment. Following advocacy from DND*i* and our partners, WHO added mycetoma to its list of NTDs in 2016 – an important step in raising awareness of the disease and encouraging investment in research for diagnostics and treatments that can be easily used in rural areas.

Our goal is now to develop a new treatment for mycetoma that can prevent devastating amputation and disability – and to ensure access for all people in need.

Fosravuconazole

The Mycetoma Research Centre, a WHO Collaborating Centre in Khartoum, Sudan, began enrolling patients in the first-ever double-blind, randomized clinical trial for fungal mycetoma treatment in 2017. The trial is studying the efficacy of treating moderate-sized lesions with a weekly dose of fosravuconazole over a period of 12 months, compared to daily treatment with itraconazole, the current standard of care.

In 2020, with 104 participants of a target of 165 enrolled in the study, recruitment was placed on hold while a second interim analysis is prepared. Once the analysis is completed in 2021, the clinical trial may be terminated or may progress until full recruitment is completed in 2022. Discussions with regulatory authorities in Sudan to obtain conditional approval for compassionate use of the drug will also begin in 2021.

Identifying new drug candidates: MycetOS

The Mycetoma Open Source project (MycetOS) uses an 'open-source pharma' approach to discover new treatments targeting *Madurella mycetomatis*, the most common cause of fungal mycetoma. Participating researchers engage through community-driven, in-kind scientific contributions, with all ideas and results published immediately in real time to an open-access database, free of intellectual property constraints. In 2020, MycetOS improved web-based options for sharing and tracking data, and identified additional 'hit' starting points with potential against *Madurella mycetomatis* via screening of the open-source Pandemic Response Box pioneered by the Medicines for Malaria Venture and DND*i*.

HIV

Ensuring access to life-saving treatment for children and people with advanced HIV

The antiretroviral treatment revolution has enabled millions of people with HIV to live long and healthy lives. But a lack of appropriate treatments for children and people with advanced HIV continues to leave many behind – almost half of the nearly 2 million children living with the disease are not accessing treatment. And hundreds of thousands of people still die each year from HIV-related opportunistic infections for which affordable and easy-to-take medicines are still lacking.

FIND OUT MORE

HIV statistics

50%
of children living with HIV will die before their second birthday without treatment

ONLY **53%**
of children are receiving life-saving treatment

180,000
people die every year from HIV-related cryptococcal meningitis

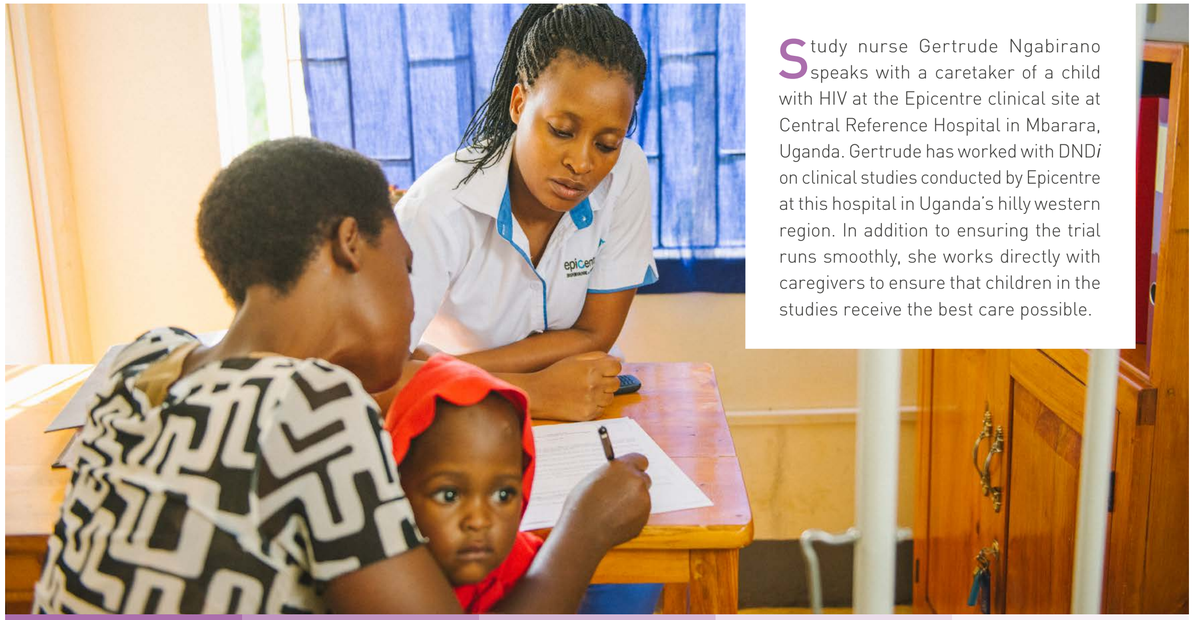
The push for progress

Until recently, the only treatment options for children with HIV consisted of awful-tasting syrups that are difficult for kids to take. With our partners, DND*i* developed an easy-to-administer '4-in-1' formulation for infants and young children. Much simpler for children and caregivers alike, it contains four antiretrovirals in one capsule of strawberry-flavoured granules that can be sprinkled on food. Our teams have also initiated work to address access barriers to first-line treatment regimens and to develop improved, simpler formulations of existing treatments for cryptococcal meningitis, a leading killer of people with HIV.

Our goal is now to make sure the 4-in-1 is registered and available to children who need it, while promoting access to all available child-friendly treatment formulations and improving access to safe, effective, and affordable treatments for cryptococcal meningitis. And we continue to explore new ways to address neglected R&D needs for serious HIV-related opportunistic infections (advanced HIV) and HIV treatments for neonates, children, and adolescents.

A strawberry-flavoured '4-in-1' treatment for infants and young children

Together with our manufacturing partner, Cipla Ltd, DND*i* has completed development of a '4-in-1' combination HIV treatment specifically designed for infants and young children. The easy-to-administer, strawberry-flavoured formulation requires no refrigeration and is a great improvement over the current treatment option: a bitter-tasting syrup with high alcohol content that needs to be kept in a cold chain. The regimen comes in the form of granule-filled capsules that parents and caretakers can administer easily by opening the capsules and sprinkling on soft food, water, or milk.



Study nurse Gertrude Ngabirano speaks with a caretaker of a child with HIV at the Epicentre clinical site at Central Reference Hospital in Mbarara, Uganda. Gertrude has worked with DND*i* on clinical studies conducted by Epicentre at this hospital in Uganda's hilly western region. In addition to ensuring the trial runs smoothly, she works directly with caregivers to ensure that children in the studies receive the best care possible.

Developed with financial support from Unitaid, Agence Française de Développement (AFD), and others, the 4-in-1 was submitted to the US Food and Drug Administration for tentative approval in late 2019 and re-submitted for full approval in mid-2020.

In Uganda, DND*i* and partners completed the clinical phase of the LOLIPOP study, which will provide clinical data on the 4-in-1 in infants and young children living with HIV.

Confronting a deadly HIV co-infection

About 180,000 people die every year from HIV-related cryptococcal meningitis, one of the leading causes of death in people with advanced HIV. The drug flucytosine is a key component of WHO-recommended first-line treatment for HIV-related cryptococcal meningitis; however, standard formulations of the drug – delivered in four divided doses per day – are poorly adapted for use in under-staffed and over-burdened hospitals.

Together with partners, DND*i* worked in 2020 to deliver a simpler, sustained-release formulation of flucytosine. A new project consortium was established with support from EDCTP. An application to conduct the first Phase I study of the new formulation was also submitted to the South African Health Products Regulatory Authority for review, in collaboration with FARMOVS, a partner clinical research organization that will lead the study in South Africa ahead of later Phase II studies planned for Tanzania and Malawi.

Flucytosine is not yet registered for use in most African countries. Alongside efforts to deliver a new formulation of the drug adapted for use in resource-limited settings, partners also initiated efforts in 2020 to facilitate uptake of the drug, including through the development of field-adapted educational tools and a framework for enabling comprehensive access.

HEPATITIS C

Accelerating access to affordable treatments and supporting global elimination efforts

Hepatitis C (HCV) is a potentially fatal disease that is often called a 'silent killer' because it can go decades without detection while causing serious liver damage and even liver cancer. There are 58 million people living with HCV worldwide, despite the existence of safe, simple, and highly effective DAA treatments that can cure the disease in weeks. Yet just 13% of people with HCV globally have benefited from these treatments to date, largely due to poor access to simple diagnostic tests and because the drugs have been priced out of reach.

FIND OUT MORE

> "We are so happy for the patients. They have been waiting for a treatment for so long. Now, we can tell them: I have the treatment for you right now."
>
> **Datuk Dr Muhammad Radzi Abu Hassan**, National Head of Gastroenterology and Hepatology, Ministry of Health, Malaysia

HEPATITIS C statistics

58 MILLION
people are living with HCV globally

ONLY **13**%
have had access to treatment

800
people die from HCV every day

The push for progress

Together with our partners, DND*i* developed ravidasvir for use as part of an effective, simple-to-use, affordable treatment for HCV that can increase access and minimize financial burden on patients and health systems. We have also joined with government and civil society groups in Malaysia, industry partners, and FIND, the global alliance for diagnostics, to pioneer the 'test-and-treat' strategies needed to scale up access to diagnosis and treatment and realize ambitions to eliminate the disease worldwide.

Our goal is now to ensure access to ravidasvir for people still waiting for a cure while expanding our partnerships to bolster affordable and sustainable supply of all DAAs and foster the political will and financing needed for wide-scale roll-out of life-saving testing and treatment.

An affordable new treatment, thanks to South-South cooperation

DND*i* and Pharmaniaga Berhad submitted ravidasvir for regulatory approval with Malaysia's National Pharmaceutical Regulatory Agency (NPRA) in late 2020. In June 2021, the NPRA granted conditional registration for the new safe, effective, and affordable HCV medicine developed in partnership by DND*i*, the Malaysian Ministry of Health, Pharco Pharmaceuticals, Pharmaniaga, Presidio Pharmaceuticals, and MSF.

Recruitment for the second stage of DND*i* and partners' STORM-C-1 trial to evaluate the safety and efficacy of ravidasvir was completed in September 2020, with a total of 302 participants enrolled (177 in Malaysia and 125 in Thailand). Preliminary results from follow-up visits confirm the efficacy and safety results seen in the earlier stage of the trial, which were published in *The Lancet Gastroenterology and Hepatology*.

Building from the shared commitment, public-private partnership, and South-South cooperation that enabled the development of ravidasvir, our teams are now joining with partners to (1) raise decision-makers' awareness of HCV and the opportunity for elimination, (2) design sustainable financing mechanisms for treatment scale-up in LMICs, (3) support uptake of simplified HCV diagnostic tools and strategies, and (4) accelerate access to all simple and affordable DAA treatments in high-burden LMICs.

Waiting for the cure

When Malaysian farmer Ng Song Ping was diagnosed with hepatitis C, his doctor told him that he would have no choice but to wait. Song Ping waited a decade, because revolutionary new drugs were priced out of reach for Malaysia. In our short film, we tell Song Ping's story – a story repeated countless times in Malaysia and beyond – and show how a remarkable group of partners from Egypt and Malaysia teamed up with DND*i* to deliver an affordable hepatitis C treatment that can finally bring hope to those waiting for a cure.

COVID-19

Accelerating research, advocating for accountability, and preparing for future pandemics

We publish this report against the backdrop of a devastating global pandemic that has claimed millions of lives, disrupted livelihoods, undermined critical gains in global health and development, and shone a glaring light on the health consequences of systemic racial and economic inequalities within and between countries. The global response to the COVID-19 pandemic is enabling major scientific advances and the development of new medical tools at unprecedented speed. But it has also thrown into sharp relief the limited commitment to prioritizing and financing research needs in resource-limited settings – for COVID-19 and neglected diseases more broadly – and the lack of preparedness and globally agreed rules to ensure both transparency and equitable access to life-saving medical tools.

FIND OUT MORE

The push for progress

From the start of the pandemic, DND*i* teams have been working to leverage our experience in public-interest R&D and partnerships across LMICs to help ensure all people have access to the medical innovations needed to control the pandemic, protect health, and save lives – no matter where they live.

Together with partners, we have been advancing multi-pronged efforts to accelerate research and equitable access to new health tools in resource-limited settings, including:

- Advocating and collaborating for the advancement of COVID-19 research driven by the needs of low-resource settings;
- Coordinating clinical research for urgently needed treatments for mild-to-moderate COVID-19 to enable early treatment and prevent spikes in hospitalizations that could overwhelm fragile and already overburdened health systems;
- Identifying new drug candidates for the treatment of mild-to-moderate COVID-19 and future coronaviruses; and
- Calling for accountability from governments, industry, and the research community to ensure that COVID-19 R&D is driven by the public interest and that new health tools reach everyone who needs them.

Our goal is now to develop and deliver therapeutic solutions for COVID-19 and other pandemic-prone diseases while helping to bolster pandemic preparedness and response, with a focus on neglected and marginalized communities.

COVID-19 Clinical Research Coalition

In April 2020, DND*i* co-launched the COVID-19 Clinical Research Coalition as part of a global effort to facilitate and accelerate research that would provide evidence on COVID-19 prevention, diagnosis, and case management in resource-limited settings – research to meet the needs of LMICs, driven by clinicians and scientists in LMICs, in a context where global health priorities have been largely driven by the needs of high-income countries. In a comment published in *The Lancet* the same month, a group of scientists, physicians, funders, and policymakers from over 70 institutions in more than 30 countries pledged their support for the initiative.

DND*i* hosts the secretariat of the coalition, which by mid-2021 has brought together more than 800 members from 88 countries (nearly 70% from LMICs), including almost 500 representatives of 230 member institutions – each committed to: (1) leveraging their expertise for high-impact COVID-19 research in low-resource settings; (2) championing equitable and affordable access to COVID-19 vaccines, diagnostics, and treatment; and (3) promoting open sharing of research knowledge and data.

In the coalition's first year, members have formed 13 topic-specific working and advisory groups, actively consolidating expertise and capacity to address specific needs identified by stakeholders in low-resource settings. In areas spanning data management and sharing, clinical epidemiology, the social sciences, and more, members are playing an instrumental role in advising researchers on common challenges in their respective fields, driving dialogue and consensus on priority research questions, and developing urgently needed studies to fill those gaps. Working groups also share topic-specific resources and organize webinars for scientific exchange and problem-solving.

The coalition has also established a protocol repository to support other researchers to better understand the design and methodologies of proposed and existing studies, to standardize endpoints, and to accelerate research planning by providing examples that may be adapted for other contexts.

COVID-19

Bolstering drug discovery for COVID-19 and future coronaviruses

DND*i*'s drug discovery team began work in the second half of 2020 to leverage our network for open and collaborative drug discovery to identify new drug candidates for COVID-19 and future coronaviruses.

In the shorter term, our partnerships are working to identify potential drug candidates from known antivirals – beginning with the *in vitro* and *in vivo* experimental work needed to provide supporting pre-clinical evidence. We are focusing mainly on compounds that have a direct-acting antiviral (DAA) profile and on combinations of antivirals and anti-inflammatories that could be effective in treating COVID-19 at its multiple stages of progression. *In vivo* experiments to obtain pre-clinical data on several known antivirals were started in late 2020, and at least three additional potential treatments will be investigated in 2021.

Over the longer term, our teams are also focusing on discovering all-new antiviral drugs. As work to deliver a new clinical candidate can take at least two to four years, it is essential that drug discovery efforts to prepare for the next pandemic are started early. We are working to contribute to pandemic preparedness through longer-term initiatives to discover novel antiviral drug candidates for the treatment of SARS-CoV-2, future generations of coronavirus, and potentially other pandemic-prone viruses.

Our push to accelerate drug discovery for COVID-19 has also included ensuring COVID-19 researchers' access to the Pandemic Response Box, opening access to the compound library of our Lead Optimization Latin America (LOLA) project, and linking student researchers in our Open Synthesis Network to COVID-19 drug discovery efforts via the COVID Moonshot project.

ANTICOV: Addressing the urgent need for treatments that can prevent hospitalization

Surges in cases of severe COVID-19 have wreaked havoc on healthcare systems in settings with limited intensive care facilities and insufficient access to oxygen therapy. Treating mild and moderate cases of COVID-19 before they become severe could help to save lives and reduce shortages of essential resources. However, the vast majority of research studies to evaluate COVID-19 treatments have taken place in high-income countries, and most have focused on the needs of hospitalized patients with severe COVID-19.

To address gaps in research for treatments adapted for use in resource-constrained settings and less severe forms of COVID-19, DND*i* and a consortium of 25 organizations from Africa and around the world have joined forces to implement the ANTICOV clinical trial across 19 sites in 13 African countries*. Our aim is to identify one or two treatments for mild and moderate cases of COVID-19 that can limit progression to severe disease.

Launched in November 2020, ANTICOV will recruit up to 3,000 patients, testing potential treatments using an innovative and flexible 'adaptive platform' trial design that allows for treatments to be added or removed as new evidence emerges. ANTICOV is initially focused on testing 'repurposed' drugs that are known to be safe and effective against other infectious diseases. The trial is also poised to serve as a platform for evaluating future study regimens composed of entirely new drug candidates.

At the time of publication, DND*i* and our partners are examining the possibilities of extending ANTICOV to Latin America and conducting a similar trial in India.

* Major funding for ANTICOV is provided by the German Federal Ministry of Education and Research (BMBF) through KfW and by the global health agency Unitaid as part of ACT-A. Participating countries at time of launch: Burkina Faso, Cameroon, Côte d'Ivoire, DRC, Equatorial Guinea, Ethiopia, Ghana, Guinea, Kenya, Mali, Mozambique, Sudan, Uganda.

Advocating for accountability

The scientific response to COVID-19 is enabling major advances and the development of new health technologies, particularly vaccines and diagnostics, at unprecedented speed. For some populations and some countries, increased access to these essential tools means the tide of loss and disruption brought by the pandemic may be at least temporarily waning. But for millions of people in countries and communities still without access, new waves of COVID-19 continue to claim lives and cause terrible suffering.

DND*i* has long used our experience in needs-driven R&D to advocate for the public responsibility and public policies required to meet the medical needs of the most neglected patients. In 2020, we called on governments, donors, industry, and the research community to take concrete steps to ensure that unprecedented public and philanthropic funding for COVID-19 research would result in affordable health tools that reach everyone who needs them. We also supported the WHO Solidarity Call to Action for equitable global access to COVID-19 health technologies – committing to implement its recommendations to accelerate COVID-19 research in LMICs – and worked to build support for South Africa and India's proposal to the World Trade Organization for a time-limited waiver of the Trade Related Aspects of Intellectual Property Rights (TRIPS) agreement.

The global response to COVID-19 has shown that 'business-as-usual' approaches to global health innovation and access continue to threaten timely and equitable access to the fruits of scientific progress. We will continue to call for the public leadership and international cooperation required to correct course in this pandemic and appropriately prepare for pandemics to come.

NEW TREATMENTS IN CLINICAL DEVELOPMENT

A total of 22 clinical trials in 2020:

6 clinical trials **started**

15 clinical trials **ongoing**

1 clinical trial **completed**

8 diseases

83 clinical trial **sites**

28 countries

3,140 patients enrolled

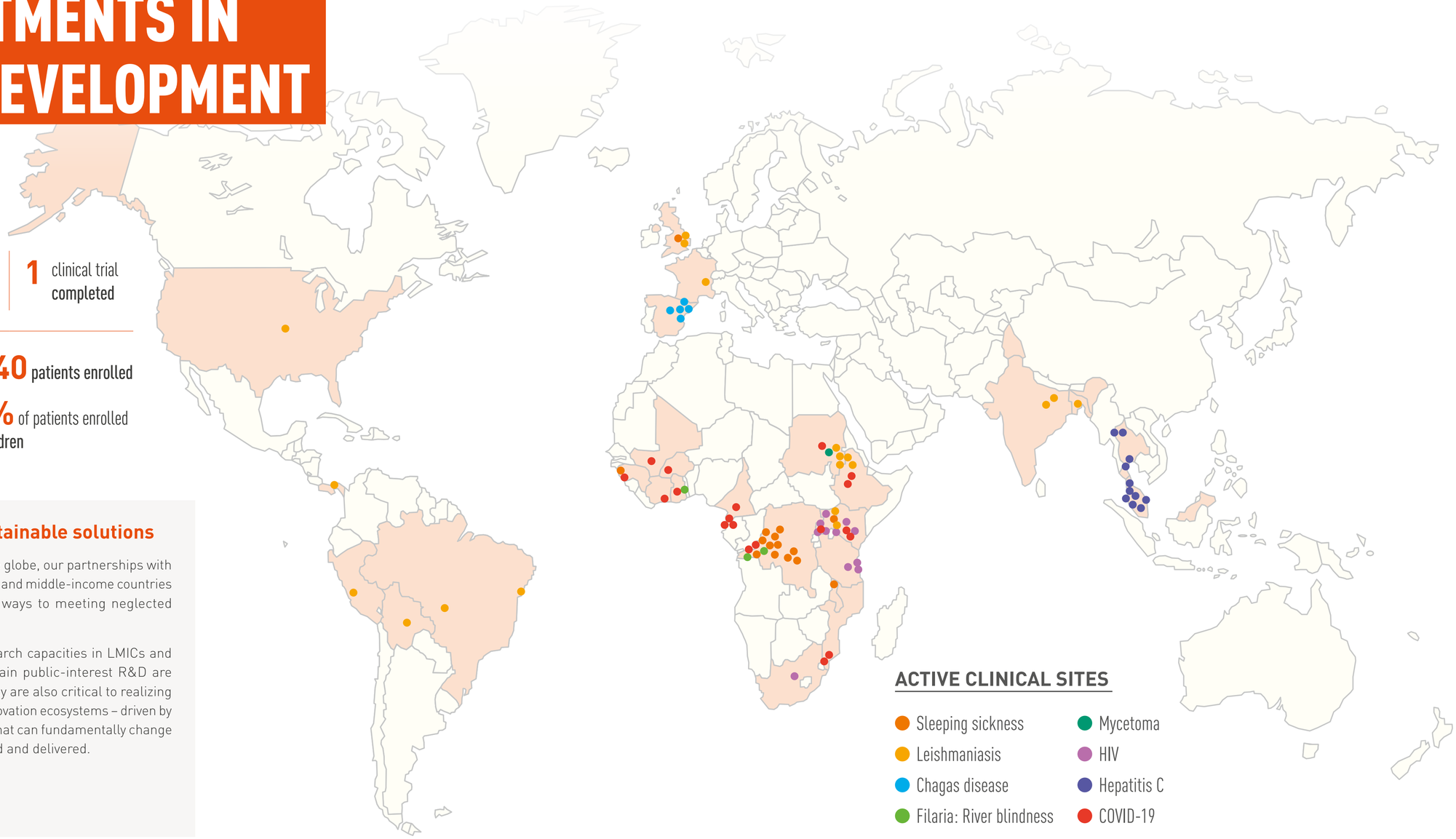
49% of patients enrolled are children

Fostering inclusive and sustainable solutions

While DND*i*'s strategic alliances span the globe, our partnerships with public health and scientific experts in low- and middle-income countries (LMICs) contribute in unique and vital ways to meeting neglected patients' needs.

Initiatives to utilize and strengthen research capacities in LMICs and support networks of excellence to sustain public-interest R&D are central to DND*i*'s virtual R&D model. They are also critical to realizing our ultimate objective of fostering new innovation ecosystems – driven by scientific leaders in affected countries – that can fundamentally change how R&D in the public interest is realized and delivered.

FIND OUT MORE



OUR R&D PARTNERS

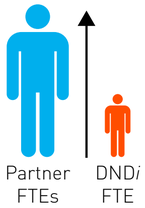
DND*i* is deeply grateful to our 200+ R&D partners worldwide, whose commitment has sustained our work since 2003.

Collaboration is an essential part of DND*i*'s model

We cannot carry out our work without the engagement of our public and private partners. Acting as a 'conductor of a virtual orchestra', we leverage and give value to our partners' specific assets, capacities, and expertise.

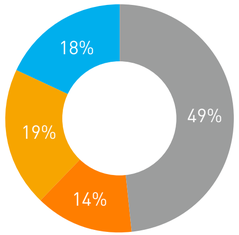
In 2020, for each DND*i* FTE,* we could count on more than four FTEs in partner organizations globally, with a 14:1 ratio for African partners.

Global FTE ratio – 4.6:1

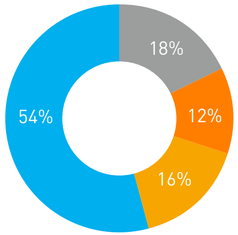


Our proximity to the needs of patients and affected communities is critical and can only be achieved through building trusting and equal partnerships with local clinicians, scientists, and experts, as well as patient and community/civil society groups in affected countries. Over half of the partner institutions we work with are in LMICs, and 82% of partner FTEs are in LMICs. Some 66% of all R&D partner FTEs are in Africa.

R&D third parties by location



R&D third-party FTEs by country income



- High income
- Upper middle income
- Lower middle income
- Low income

Creating value through partnership

DND*i* harnesses the best of the public, private, non-profit, academic, and philanthropic sectors to bring the best science to the most neglected and drive knowledge creation through open and collaborative approaches to medical innovation.

Our closest partnerships are with the organizations that founded us. Our academic and public health research institute founding partners from Brazil, France, Kenya, India, and Malaysia enable us to leverage expertise and technical investment across the globe. MSF's field work informs DND*i*'s R&D priorities, and we collaborate on clinical trials and share scientific and policy expertise. As the world's normative agency for global health, our strategic partnership with WHO is central to our mission.

From drug discovery and clinical research to ensuring the treatments we develop reach patients in need, we could not deliver life-saving medical innovation without the partners who power our progress.

We would like to take this opportunity to highlight the pharmaceutical companies* that contributed to DND*i* projects in 2020:

AbbVie, USA; Anacor Pharmaceuticals (now Pfizer Inc.), USA; Ascletis BioScience Co., Ltd., China; Astellas Pharma, Japan; AstraZeneca, UK and Sweden; Atomwise, USA; Bayer, Germany; Celgene Corporation (now Bristol-Myers Squibb), USA; Cipla Ltd., India; Daiichi Sankyo, Japan; Eisai Co., Ltd., Japan; Eurofarma, Brazil; GlaxoSmithKline, UK and Spain; Johnson & Johnson, USA; Laboratorio Elea Phoenix, Argentina; Merck KGaA, Germany; Mitsubishi Tanabe Pharma Corporation, Japan; Viatris (through its subsidiary Mylan), India; Novartis, Switzerland and USA; Pharco Pharmaceuticals, Inc., Egypt; Pharmaniaga, Malaysia; Presidio Pharmaceuticals, USA; Sanofi, France; Shionogi & Co., Ltd., Japan; Takeda Pharmaceutical Company Limited, Japan; Zoetis (formerly Pfizer Animal Health), USA.

* Does not include service providers

* Staff in full-time equivalents

Industry partners and service providers | Universities and research centres | Non-profit organizations, NGOs, and networks | Healthcare providers | Ministries of health and governments

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Bennett Shapiro
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John Reeder
Permanent observer; WHO-TDR Special Programme for Research and Training in Tropical Diseases, Switzerland

FIND OUT MORE

Note: Lists include membership from January to December 2020, unless otherwise specified

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CONTRIBUTIONS AND EXPENDITURE

In 2020, DND*i* secured EUR 56 million in funding from public and private institutions and individuals, despite a volatile donor environment, bringing the total to EUR 676 million since its inception in 2003.

New funding in 2020

DND*i* secured EUR 56 million in new funding in 2020. Funding successes and DND*i*'s wide range of supporters are evidence of DND*i*'s attractive value proposition to global donors seeking to leverage innovation for enhanced access to health, especially in low-resource settings.

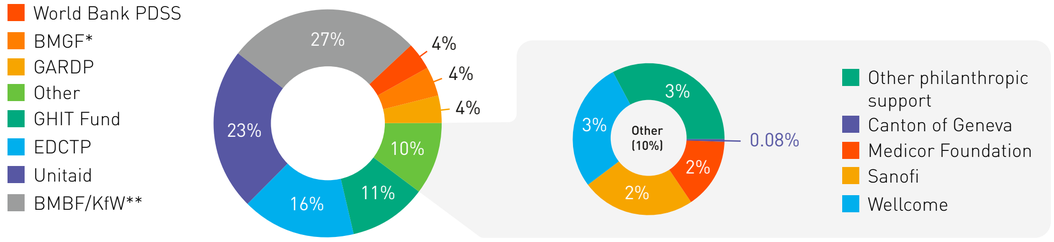
In 2020, the Swiss Agency for Development and Cooperation (SDC) was the only public institution to announce multi-year unrestricted funding support for DND*i*. Thus, the funding perspective for the coming years is less clear than anticipated, which could lead to implementation delays if donor decisions are further postponed.

The COVID pandemic has affected DND*i*'s relationship with its funding partners in several ways.

DND*i* was called to engage in COVID-19 response activities but was mindful to protect funding secured for NTDs and other viral diseases, therefore we focused on securing new and dedicated COVID-19 R&D support while sustaining investments in our historical portfolio.

The focus of the official development assistance donor community on COVID-19 allowed DND*i* to secure support for our pandemic response activities but hindered the conclusion of funding renewals while limiting commitments from new potential partners.

Source of new funding secured in 2020 (EUR 56 million)



* Bill & Melinda Gates Foundation

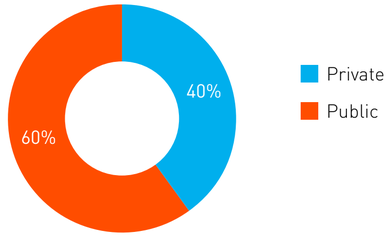
** Federal Ministry of Education and Research (BMBF) through KfW

Funding since 2003

The public/private balance of funding remains stable, while DND*i* is experiencing a decreasing trend in unrestricted funding linked to delays in the renewal of official development assistance support.

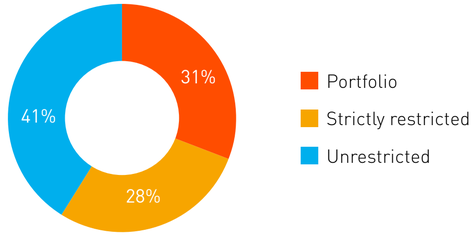
Share of public/private funding (2003-2020)

on total funding of EUR 676 million



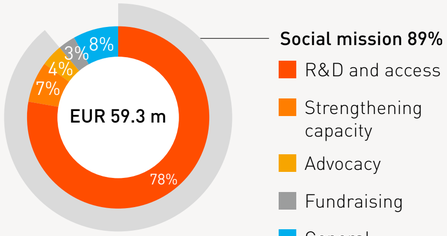
Donor restrictions (2003-2020)

on total funding of EUR 676 million



2020 expenditure totalled EUR 59.3 million, 89% of which was on our social mission.

2020 expenses



More information on donor contributions and DND*i* expenditure is available in DND*i*'s 2020 Financial and Performance Report.

A WORD OF THANKS

DND*i* has now delivered nine new treatments* for six neglected diseases. Every contribution is essential to advancing DND*i*'s mission and goals. We are deeply grateful to the following key donors for their support in 2020.

A complete list of all DNDi's donors since 2003 is available on our website.

FIND OUT MORE

Public institutional support

- Brazil - Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP)
- Brazil - Ministry of Health
- Canada - International Development Research Center (IDRC)
- DRC - Ministry of Health of the Democratic Republic of Congo (through the Projet de Développement du Système de Santé (PDSS) funded by the World Bank)
- European Union - European and Developing Countries Clinical Trials Partnership Association (EDCTP2 Programme)
- European Union - Horizon 2020 Research and Innovation programme
- Foundation for Innovative New Diagnostics (FIND) (supported by Unitaid)
- France - French Development Agency (AFD)
- Germany - Federal Ministry of Education and Research (BMBF) through KfW
- Japan - Global Health Innovative Technology Fund (GHIT Fund)
- Malaysia - Ministry of Health
- The Netherlands - Dutch Ministry of Foreign Affairs (DGIS)
- Portugal - Fundação para a Ciência e a Tecnologia (FCT)
- Switzerland - Innosuisse, Swiss Innovation Agency
- Switzerland - Republic and Canton of Geneva, International Solidarity Service
- Switzerland - Swiss Agency for Development and Cooperation (SDC)
- UK - UK aid
- Unitaid

Private support

- Anna-Maria and Stephen Kellen Foundation
- Associação Bem-Te-Vi Diversidade
- Bennett Shapiro and Fredericka Foster
- Bill & Melinda Gates Foundation
- Bristol-Myers Squibb Company
- Brian Mercer Trust
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- Jeff Nelson and Betsabe Aristud-Carrillo
- Kristin Ecklund
- Leo Model Foundation
- Margaret Golden, MD, MPH
- Médecins Sans Frontières / Doctors Without Borders
- Médecins Sans Frontières-Transformational Investment Capacity (MSF-TIC)
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- Wellcome
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- Anonymous individuals and organizations

* As of July 2021

Best science for the most neglected

A non-profit research and development organization, the Drugs for Neglected Diseases *initiative* (DND*i*) works to deliver new treatments for neglected patients, those living with Chagas disease, sleeping sickness (human African trypanosomiasis), leishmaniasis, filariasis infections, mycetoma, paediatric HIV, and hepatitis C. DND*i* is also coordinating a clinical trial to find treatments for mild-to-moderate COVID-19 cases in Africa. Since its inception in 2003, DND*i* has delivered nine new treatments to date, including new drug combinations for visceral leishmaniasis (kala-azar), two fixed-dose antimalarials, and DND*i*'s first successfully developed new chemical entity, fexinidazole, approved in 2018 for the treatment of both stages of sleeping sickness.

We innovate to save lives

Discovering and developing urgently needed treatments for neglected patients and working to ensure they're affordable, available, and adapted to the communities who need them.

We foster sustainable solutions

Working hand in hand with partners in low- and middle-income countries to power our progress and strengthen innovation ecosystems that put people's needs first.

We advocate for change

Speaking out for policy change to enable more effective and equitable R&D and access to the fruits of science for all people, no matter their income or where they live.

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DNDi
Drugs for Neglected Diseases *initiative*